to the acceptance of environmental effects on behavioral in the 1950s and 60s, and now back again. The chapter ends, though, with a soporific flowchart depicting the scientific process by which one teases out genetic and environmental influences on behavioral traits. Stephanie Sherman and Irwin Waldman then pick up the torch and succinctly describe the statistical approaches used to find genes involved in behavioral traits.

For me, the strongest feature of the book was the two chapters (by Mark Rothstein and Lori Andrews) that dealt directly with the legal implications of behavioral genetics. Indeed as much of this topic was new to me, I could easily have read an entire book on the subject. Behavior genetics in the context of the criminal justice system is a particularly compelling issue. If we embrace genetic determinism, or for that matter, cultural determinism, where is the room for free will? Culpability in criminal law requires a voluntary wrongful act and the mental state to realize that the act is wrongful. If a genetic defense is used, other issues are raised as well. Who will pay for the genetic testing if the defense grasps at genetic straws? If a jury decides that a defendant is innocent on the grounds of genetic predisposition, what are the implications for others with similar genetic predisposition? Will they be stigmatized or feared or even kept under surveillance?

While many of the authors are correct to point out epigenetic and environmental influences on behavior, only one took great pains to argue against genetic reductionism. In his chapter, Kenneth Schaffner asks whether any behavioral trait can have a purely genetic explanation and goes on to answer "no." His argument—that genes encode proteins which interact with other proteins, and that neurons, not genes, control behavior—struck me as clumsy and semantic.

Multiauthor compilations such as this one inevitably suffer from a number of problems. The writing is spotty, and there is considerable overlap between some essays. At least two authors describe the circuitous history of behavioral studies on schizophrenia, for example. However, the most dissatisfying aspect of the book is that the most recent literature citations are from 1997, while the publication date is 1999. Since the reader is now primed to care about the genetics of schizophrenia, she wants to know "how did it all turn out in the end?"

Despite these flaws there is a place on every human geneticists bookshelf for *Behavioral Genetics*. Not only are parts of it well worth reading, it is chock full of illustrative annotations and references.

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Cells and Genes in Molecular Therapeutics

Ex Vivo Cell Therapy
Edited by Klaus Schindhelm and Robert Nordon
London: Academic Press (1999). 356 pp. $79.95

The past year has seen the extremes of success and setbacks in the infant field of gene therapy. Overshadowed by the initial occurrences of serious complications reported in gene therapy trials was the first report suggesting real success in the use of this technology for the treatment of a monogenic disorder (Carazzana-Calvo et al., Blood *94*, 367a, 1999). In addition to ongoing criticisms of the focus on human trials in this area by some in the scientific community, the alleged oversights in the conduct of specific trials and deficiencies in patient safeguards at several prominent academic centers has been a setback for the field as a whole. The field still suffers from unrealistic expectations encouraged in part by some "gene therapists" in the 1980s. The focus on gene therapy technology has overshadowed truly remarkable advances made over the last two decades in the use of cellular therapies, particularly bone marrow transplantation and adoptive immunotherapy. However, there can be little doubt that steady progress has been made in the technology of gene transfer over this same time period, and that the application of gene transfer technology to the treatment of human disease will become an important component of medical therapies in the future.

The underlying theme of *Ex Vivo Cell Therapy* is that the use of cells and genes in human therapy represents a sufficiently complicated application as to require working collaborations between clinicians, biologists, engineers, and technicians. The multiauthored chapters of this book thus attempt to provide a broad overview of the current knowledge of hematopoiesis, immunology, and transplantation biology, as well as the state of the art technologies of vectors, hematopoietic cell separation and purification, and cell expansion using "clinical grade" bioreactors. The book will be useful to anyone whose expertise is in one of these interdependent fields. The chapters vary in details and in quality, with the inevitable overlap in some areas (particularly noticeable in multiple chapters which address ex vivo expansion of hematopoietic stem cells).

Hematopoiesis is the process in which billions of leukocytes, erythrocytes, platelets, immune effector cells, and the other cellular constituents of the blood are produced every hour of an individual's lifetime. This enormous cell production is accomplished within narrow limits of normal cell numbers found in the blood and tissues and yet bone marrow production of blood cells must be able to increase rapidly in response to stress and insult. Beginning with the first description of the colony-forming cells (both in vitro and in vivo) that defined hematopoietic progenitor cells in the 1960s, the understanding of proteins controlling the growth and differentiation of these cells has steadily increased. Significant therapeutic reagents have already arisen from this understanding. More recently, the use of molecular and cell biological methods as well as gene targeting methods have also begun to elucidate the pathways involved in receptor signaling and transcriptional regulation of the lineage-specific genes that determine cell fate of blood cells. In spite of this progress, the factors that regulate homeostasis and differentiation of hematopoietic stem cells (the most primitive cells in bone marrow from which all blood cells are derived) are to date largely unknown.

In superb initial chapters, pathways involved in growth factor receptor signaling in hematopoietic cells are discussed, including JAK/STAT, Ras, phospholipase C, and recently described inhibitory pathways. Also, the transcriptional regulation of genes required for hematopoietic cell differentiation, such as SCL, GATA, and AML-1, is reviewed. Increasingly, as in other cell systems, cell adhesion is becoming appreciated as playing a role in signaling (not only localization) in hematopoietic cells; this topic is covered in several additional chapters. Conceptually, these chapters build a foundation for understanding both future targets of molecular interventions and the microenvironment requirements for large-scale manipulations of hematopoietic cell products.

Over the last 30 years there has been a significant increase in the use of bone marrow transplantation for the treatment of malignant, genetic, and in some cases autoimmune diseases. Increasingly, bone marrow cells are being replaced with mobilized peripheral blood or umbilical cord blood as sources of transplantable stem cells. The use of allogeneic, autologous, and cord blood transplants is reviewed in helpful middle chapters. The authors have done, with rare exceptions, a nice job of summarizing the use, advantages, and disadvantages of each of these approaches in current therapies. In so doing, the chapters provide a brief overview of increasingly complex data from multiple sources with respect to outcomes and complications. Two noticeable oversights are the lack of discussion of the emerging use of haploidentical (usually parenteral or sibling) transplants in the treatment of malignant disesase and the use of so-called "mini" or submyeloablative transplants, which may have an enormous impact on the future treatment of nonmalignant diseases.

Cellular adoptive immunotherapy entails the transfer of effector cells of the immune system, usually CD4 or CD8 lymphocytes for the treatment of malignant diseases or infections. Remarkable progress has been made in this area, including development of effective adoptive transfer methods to treat leukemia, Epstein-Barr virus (EBV)-associated lymphoma and melanoma. Additional applications include treatment of serious, often fatal, EBV and cytomegalovirus infections in the immunocompromised host. In another excellent chapter, the basic biology of lymphocyte-mediated immunity is discussed, and this and other clinical applications are reviewed, including data on ongoing clinical trials. Future applications in human immunodeficiency virus (HIV) treatment are considered in light of the ability of natural-host T cell response to only partially control HIV virus replication. Such future applications may well require genetic modification of T lymphocytes. Ex vivo expanded dendritic cells may also prove useful in future therapies.

Success of cellular and gene therapies in the clinical setting will require translating laboratory-based methods into cell production and modification processes in large scale with standards of safety similar to other therapeutics. In the latter chapters of this book, the editors have attempted to compile several chapters reviewing core technologies required for clinical applications of ex vivo cell therapies. These technologies include cell separation, cell expansion, and gene modification. The goals of cell separation include selection for "target cells" and passive elimination of contaminating tumor or effector cells. Cell separation, by purifying a rare target cell population, provides the added benefit of reducing the amount of reagents and simplifying manipulations (and therefore potential complications) required for downstream processes. The goals of cell expansion include both manipulating the cellular constituents of the final cell product and facilitation of transplants using a limited initial number of cells. Clearly the efficacy of these emerging technologies is yet to be shown in the clinic. The regulatory aspects of cell purification and expansion technology are discussed. Commercial systems of cell purification and cell expansion are covered, although this information is derived from scientists at only two biotechnology companies while several other relevant proprietary approaches are not discussed.

Gene delivery technology, including virus vectors, liposome, particle-mediated, electroporation, and direct DNA injection are reviewed. To accomplish this in limited space required a brief treatment of each technology covering basics without significant details. Advantages and disadvantages of each technology are noted providing a useful guideline to those not currently in the field. No discussion of regulatory issues as these relate to human gene therapy trials is present. Workers in the field will recognize that these regulations are significant in both volume and detail, but their inclusion at least in summary form would have added to the overall usefulness of this book.

Understanding the molecular processes that control cell growth and differentiation is a major goal of cell and molecular biologists. Application of this knowledge to defining the molecular defects causing human diseases has been the task of scientists in the past 20 years, beginning with the characterization of the molecular basis of hemoglobinopathies. Over the next several decades the development of strategies to repair the cellular systems affected by genetic mutations will be an ongoing goal. This book provides a compact review of the basic biology of hematopoiesis and technologies being developed to manipulate hematopoietic cells either to eliminate diseased cells or to restore and augment normal function to the blood system.

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Prokaryotic Genomes: The Hidden Code

Organization of the Prokaryotic Genome
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It is evident that biology has entered a new period, sometimes called the genomics era. Genomic technologies